Development of Highly Active Anti-Leukemia Stem Cell Therapy (HALT)

Grant Award Details

Development of Highly Active Anti-Leukemia Stem Cell Therapy (HALT)

Grant Type: Disease Team Research I

Grant Number: DR1-01430

Project Objective: Original aim was to block leukemic stem cells (LSC) with small molecules or monoclonal antibodies to eradicate LSC and spare hematopoietic stem cells. This was a Collaborative Funding Partnership Program with Dr. John Dick Toronto Canada. Project successful in that the Carson team is going forward to submit an IND application for their ROR1 monoclonal antibody and Dr Dick has successfully procured Industry partnership for an extensive biomarker program for finding prognostic gene signatures in AML and other leukemia's.

Investigator:

Name:	Dennis Carson
Institution:	University of California, San Diego
Type:	PI

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Name:	Catriona Jamieson
Institution:	University of California, San Diego
Type:	Co-PI

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Name:	John Dick
Institution:	University Health Network
Type:	Partner-PI

Disease Focus: Blood Cancer, Cancer

Collaborative Funder: Canada

Human Stem Cell Use: Cancer Stem Cell

Award Value: $19,999,826

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Grant Application Details

Application Title: Development of Highly Active Anti-Leukemia Stem Cell Therapy (HALT)

Public Abstract:

Leukemias are cancers of the blood forming cells that afflict both children and adults. Many drugs have been developed to treat leukemias and related diseases. These drugs are often effective when first given, but in many cases of adult leukemia, the disease returns in a form that is not curable, causing disability and eventual death. During the last few years, scientists have discovered that some leukemia cells possess stem cell properties that make them more potent in promoting leukemia growth and resistance to common types of treatment. These are called leukemia stem cells (LSC). More than in other cancers, scientists also understand the exact molecular changes in the blood forming cells that cause leukemias, but it has been very difficult to translate the scientific results into new and effective treatments. The main difficulty has been the failure of existing drugs to eliminate the small numbers of LSC that persist in patients, despite therapy, and that continue to grow, spread, invade and kill normal cells. In fact, the models used for drug development in the pharmaceutical industry have not been designed to detect drugs or drug combinations capable of destroying the LSC. Drugs against LSC may already exist, or could be simple to make, but there has not been an easy way to identify these drugs. Recently, physicians and scientists at universities and research institutes have developed tools to isolate and to analyze LSC donated by patients. By studying the LSC, the physicians and scientists have identified the molecules that these cells need to survive. The experimental results strongly suggest that it will eventually be possible to destroy LSC with drugs or drug combinations, with minimal damage to most normal cells. Now we need to translate the new knowledge into practical treatments. The CIRM Leukemia Team is composed of highly experienced scientists and physicians who first discovered LSC for many types of leukemia and who have developed the LSC systems to test drugs. The investigators in the Team have identified drug candidates from the vigorous California pharmaceutical industry, who have already performed expensive pharmacology and toxicology studies, but who lack the cells and model systems to assess a drug's ability to eliminate leukemia stem cells. This Team includes experts in drug development, who have previously been successful in quickly bringing a new leukemia drug to clinical trials. The supported interactive group of physicians and scientists in California and the Collaborative Funding Partner country has the resources to introduce into the clinic, within four years, new drugs for leukemias that may also represent more effective therapies for other cancers for the benefit of our citizens.

Statement of Benefit to California:

Thousands of adults and children in California are afflicted with leukemia and related diseases. Although tremendous gains have been made in the treatment of childhood leukemia, 50% of adults diagnosed with leukemia will die of their disease. Current therapies can cost tens of thousands of dollars per year per patient, and do not cure the disease. For the health of the citizens of California, both physical and financial, we need to find a cure for these devastating illnesses.

What has held up progress toward a cure? Compelling evidence indicates that the leukemias are not curable because available drugs do not destroy small numbers of multi-drug resistant leukemia stem cells. A team approach is necessary to find a cure for leukemia, which leverages the expertise in academia and industry. Pharmaceutical and biotech companies have developed drugs that inhibit pathways known to be involved in leukemia stem cell survival and growth, but are using them for unrelated indications. In addition, they do not have the expertise to determine whether the inhibitors will kill leukemia stem cells. The Leukemia Team possesses stem cell expertise and has developed state of the art systems to determine whether drugs will eradicate leukemia stem cells. They have also have access to technologies that may allow them to identify patients who will respond to the treatment. The development plan established by the Leukemia Disease Team will also serve as a model for the clinical development of drugs against solid tumor stem cells, which are not as well understood.

In summary, the benefits to the citizens of California from the CIRM disease specific grant in leukemia are:

(1) direct benefit to the thousands of leukemia patients

(2) financial savings due to definitive treatments that eliminate the need for costly maintenance therapies

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